STIC-ILL

M

From: Lukton, David
Sent: Friday, December 28, 2001 2:20 PM
To: STIC-ILL

376758

David Lukton
308-3213
AU 1653
Examiner room: 9B05
Mailbox room: 9B01
Serial number: 09/508635

539324

* * * * * * * * * * * * *

L3 ANSWER 7 OF 14 MEDLINE
AN 93173012 MEDLINE
DN 93173012 PubMed ID: 1289693
TI ***Nitrogen*** ***balance*** studies in clinical nutrition.
AU Konstantinides F N

SO NUTRITION IN CLINICAL PRACTICE, (1992 Oct) 7 (5) 231-8. Ref: 56
Journal code: NCP; 8606733. ISSN: 0884-5336.

TECHNIQUES AND PROCEDURES

Nitrogen Balance Studies in Clinical Nutrition

FRANK N. KONSTANTINIDES, MS
Surgical and Clinical Nutrition Research Facility, Department of Surgery, St. Paul-Ramsey Medical Center, St. Paul

ABSTRACT: Nutrition support is recognized as an important cofactor in altering morbidity and mortality of hospitalized patients. Paramount in delivering proper nutrition support is the accurate determination of baseline metabolic and nutritional status, thus influencing necessary protein requirements. After nutritional intervention, routine laboratory monitoring is used to measure the efficacy and to reassess metabolic stress level. Accurate determination of nitrogen excretion (and nitrogen balance) remains the standard in prescribing and monitoring the protein and nutritional treatment regimen. This article examines nitrogen excretion determinations in the clinical setting, including proper collection techniques, laboratory measurements, and analyses and their effect upon nitrogen balance studies.

Although the history of enteral feeding dates back to the ancient Greeks and Egyptians, advances in scientific knowledge and technology of modern clinical nutrition have evolved only within the past 25 years.[1] Dr Stanley J. Dudrick and his colleagues performed their famous animal study in 1968 in which the total nutritional needs of beagle puppies were adequately supported by parenteral administration.[2] Protein, fat, and carbohydrate levels were supported in the puppies, and they developed in similar fashion to their counterparts that were allowed to eat ad lib from a comparable menu. The principles of this animal study were soon applied in the case of a young girl unable to ingest food on her own. Similar results were observed and recorded in this case.[3] Nutrition support is used in many hospitalized patients. It is now recognized that nutrition support, if properly administered and carefully monitored, can safely and effectively support protein synthesis in humans, resulting in positive nitrogen balance. Nutrition support cannot halt the catabolic process induced by the neurohumorally mediated metabolic stress response accompanying trauma, surgery, or burn injuries. It supplements the raw materials of anabolism in support of new proteins for wound healing and immune response.

Both standard enteral and parenteral formulas are marketed for patients, and depending upon disease- or organ-specific requirements, specialized formulas (eg, branched-chain amino acid formulas, liver failure formulas) have also become available. New formulas continue to be developed such as one containing arginine, ribonucleic acids, and omega-3 and omega-6 fatty acids, which have been shown to have a positive effect on immune function.[4]

Nutrition support is now perceived to enhance patients' preparation for surgery as well as strengthen their prescribed program of postoperative care. A connection linking perioperative nutrition support to decreased morbidity, mortality, and length of stay in the hospital is thought to exist.

To properly determine individual nutritional demands, a thorough patient evaluation must be conducted.[5-8] The evaluation can be classified into three parts. First, a medical history and physical examination including body measurements are needed. Next, chemistry panels including visceral protein markers and immunologic tests are made. Last, urine studies of the patient should be undertaken. These include nitrogen balance assessment and the determination of the creatinine height index.

Although all three facets of nutrition assessment play an important part in evaluating patient nutriture, only the urine indices required to calculate nitrogen losses and skeletal muscle mass will be addressed in this article. The nitrogen losses determined from a 24-hour urine collection with protein (nitrogen) input enable the calculation of respective nitrogen balance. Protein requirements and the efficacy of nutrition therapies may be determined from the nitrogen balance calculation. When one measures urine creatinine losses, estimates for skeletal muscle mass can be derived.[9-11]

This article reviews nitrogen balance studies and provides a definition of nitrogen balance and information regarding proper collection techniques, laboratory measurements, and analytical procedures. Finally, the

Address for reprints: Frank N. Konstantinides, Surgical and Clinical Nutrition Research Facility, St. Paul-Ramsey Medical Center and Ramsey Clinic, Building 2, Room 153, 640 Jackson Street, St. Paul, MN 55101-2595.

0884-5336/92/0705-0231$02.00/0
NUTRITION IN CLINICAL PRACTICE 7:231-238, October 1992

interpretation of nitrogen balance is addressed as it is used with other clinical parameters and sound clinical judgment in determining protein requirements.

COMPONENTS USED IN NITROGEN BALANCE STUDIES

Nitrogen balance is equal to nitrogen output subtracted from nitrogen input. A negative nitrogen balance indicates a condition, such as trauma, burn, or surgery, in which the rate of protein catabolism exceeds the rate of protein anabolism. A positive nitrogen balance is indicative of nitrogen retention, such as in pregnancy. When adjusted for changes in weight and blood urea nitrogen, positive nitrogen balance generally correlates with net protein synthesis.

Nitrogen input can easily be calculated using the relationship of protein ingested divided by 6.25, when patients are receiving a standard hospital diet. Adjustments in nitrogen values must be made for modified amino acid formulas when total parenteral nutrition (TPN) or total enteral nutrition (TEN) is used. When patients are supplemented or transferred to oral feedings, careful monitoring must be performed to accurately quantify nitrogen input.

Absolute nitrogen output determination requires the measurement of nitrogen content from bodily excrement including urine, feces, sweat, and dermal tissue. Because of the difficulties associated with the collection of waste products, urine and feces are the most commonly collected samples used to calculate nitrogen loss. In unstressed persons, 80% to 90% of the urinary nitrogen loss can be accounted for by urinary urea nitrogen (UUN).[5,7,8,12] Because of its relative ease, low laboratory cost, and rapid turnaround time, UUN analysis is often substituted for measured TUNs. The validity of this practice in the hospitalized patient will be addressed in a later section. The measured UUN is increased by 25% to account for the nonurea component of the urine, and another factor is usually added to account for nitrogen losses through stool and skin. This factor varies depending upon the individual's level of stress, diarrhea, and other variables. Burn patients have an additional, equivalent amount proportional to burn size for burn wound nitrogen losses.[13] Interinstitutional variations in adjustment factors are common practice, but these variations will alter the reliability of nitrogen balance determinations. Each institution should develop its own standard for adjustment factors. Compliance in evaluation techniques, within nutrition support teams, must occur in order to provide valid daily nutritional assessment.

EFFECT OF SAMPLE TEMPERATURE DURING COLLECTION AND STORAGE

Many standard texts suggest that 24-hour urine specimens for nitrogen excretion tests be kept on ice, followed by refrigeration. It is unclear whether the use of ice constitutes unnecessary time and expense. Several studies have been done involving temperature and its influence on the analysis of urine. Konstantinides et al addressed the issue of storing urine on ice in a study that involved 24-hour urine collections from 29 catheterized intensive care unit patients.[14,15] They concluded that neither sterile nor unsterile samples need to be kept on ice, thereby eliminating the inconvenience of iced collection in the clinical setting (Table 1).

Zlatnik conducted a study calculating the UUN ratios among 10 women with uncomplicated pregnancies.[16] He also addressed storage effects on the urine. Samples were refrigerated and reanalyzed 7 to 10 days

Table 1. Test results from 24-hour urines collected on ice (cold) versus collected at room temperature (warm) for urinary urea nitrogen, total urinary nitrogen, and creatinine*

	Group I Sterile (n = 18)	Group II Bacteria (n = 7)	Group III Yeast (n = 4)
Urinary urea nitrogen			
Warm mean ± SD	12.04 ± 7.02	12.04 ± 6.61	17.25 ± 13.08
Cold mean ± SD	12.03 ± 7.28	11.80 ± 6.11	17.16 ± 12.99
Standard values ± SE	101.08 ± 1.41	100.85 ± 3.62	99.92 ± 1.47
Correlation coefficient	0.99	0.99	0.99
Total urea nitrogen			
Warm mean ± SD	15.49 ± 8.62	14.90 ± 7.00	22.08 ± 16.09
Cold mean ± SD	15.67 ± 8.71	14.90 ± 7.28	22.08 ± 16.29
Standard values ± SE	98.59 ± 1.09	101.08 ± 2.09	100.28 ± 0.53
Correlation coefficient	0.99	0.99	0.99
Creatinine			
Warm mean ± SD	1.05 ± 0.98	1.02 ± 0.55	1.20 ± 0.34
Cold mean ± SD	1.05 ± 1.01	1.04 ± 0.58	1.22 ± 0.3
Standard values ± SE	102.25 ± 2.6	97.81 ± 2.48	103.64 ± 4.38
Correlation coefficient	0.99	0.99	0.99

* All results are given in g/24 h collection. Reprinted with permission from Konstantinides et al.[14]

after collection. Interassay variations were minimal. It was concluded that after refrigeration, stored urine samples remain stable for analysis. Konstantinides et al also addressed the storage of frozen urine for later assessment of nitrogen balance.[17] Fifty-five paired samples were obtained from intensive care unit patients. One aliquot was analyzed soon after collection, and the other was frozen and analyzed 15 months after the first. They concluded that frozen storage of samples did not significantly affect the analysis of urine.

PRESERVATIVES

Methods of preserving urine specimens can alter the values of substances in the urine used for nutrition assessment. Konstantinides et al addressed this issue in a prospective multi-armed study performed on 11 surgical/trauma patients during the acute phase of illness.[15] Twenty-four-hour urine samples were collected by free-flowing catheters. The urine collection bags were emptied every 1 to 2 hours or as deemed necessary by staff nurses. Voiding was measured by laboratory personnel, and urine was immediately transferred to collection vessels containing EDTA-sodium metabisulfite, HCl, or no preservative. These procedures were continued for a 24-hour period, at which time the no-preservative aliquot was subdivided and 6 N HCl was added to half of the aliquot until a pH of 3.0 was obtained. No significant differences were detected among the four collection techniques for TUN, UUN, or creatinine. The average standard deviation for each sample measured for UUN, TUN, and creatinine were ±1.57, ±0.80 and ±0.12 g per collection, respectively.[15] These data suggest that when 24-hour urine is collected for assessment (TUN, UUN, or creatinine) and treatment efficacy, preservative is not required.

PARTIAL VERSUS 24-HOUR COLLECTIONS

The issue of timed urine collections has been discussed by several authors[18-23] (Table 2). Twenty-four-hour urine provides the most accurate results but is inconvenient to obtain. Shorter collection periods allow a more rapid assessment of the patient's nutritional requirements and are easier to obtain. Nitrogen balance can be calculated the same day, and nutrition therapy can be implemented immediately. Although a shorter collection period can be representative of a 24-hour period, it can depend on the correlation of many variables.

Quandt et al, Record et al, and Candio et al have determined that shorter collection periods are acceptable substitutes for 24-hour collection if the nutrition rate is kept constant.[18-20] This is especially ironic because calculation of nitrogen balance itself is a chief determinant of the nutritional state of the patient. Ford et al and Lopez et al stress the need for 24-hour collections for nutritional therapy.[21,22] Although there are certain advantages of the shorter collection periods, 24-hour urine collections are the most accurate way of determining nitrogen balance. In the highly stressed patient it may be more accurate to take sequential 24-hour collections and average them over several days.

VALIDITY OF MEASURING UUN AS A SUBSTITUTE FOR TUN

Investigators have shown that urea comprises 80% of the TUN in healthy, nonstressed surgical patients.[5,7,8,12] Others have demonstrated that this percent varies widely depending upon the degree of stress, disease state, or course of illness[24-32] (K. Boehm, personal communication) (Table 3). Part of the altered

Table 2. Partial versus 24-h urine collections in hospitalized patients*

Author/Ref. no.	Year	No. of Subjects	Age	Subjects	Time	Conclusion	Comments
Candio et al[18]	1991	56		Critically ill	4, 8, 12 versus 24 h	4, 8 h, poor; 12 h, acceptable	Addresses bias, scaling
Ford et al[21]	1987	6	8 mo to 13 y	Severely stressed	4, 8 versus 24 h	Need 24 h	
Lopez et al[22]	1986	15	2 wk to 3 y	Trauma	6 versus 24 h	6 h, acceptable; 24 h, best	
Quandt et al[19]	1984	20	24 y to 84 y	SICU	2 versus 24 h	2 h, acceptable	Nutrition must be kept constant
Record et al[20]	1984	13		Surgical	6 versus 24 h	6 h, acceptable	Infusion of calories must be kept constant
Sorkness[23]	1984	5		Trauma	4, 8, 12 versus 24 h	12 h, acceptable	If 10% error is deemed acceptable

* Publication of studies that examine the accuracy of shorter timed urine collections to their 24-h counterparts from various hospitalized patients under stress conditions.

Table 3. UUN versus TUN in hospitalized patients*

Authors/Ref. no.	Year	No. of Subjects	Subjects	Age	Comments
Steinhorn et al[29]	1985	48	ICU pediatrics	1 mo–18 y	61% postop day 1 73% postop day 2 87% postop day 3
Steinhorn and Radmer[28]	1986	25	ICU pediatrics	1 mo–18 y	41% liver failure, 35% sepsis, 48% postop, 44% overall
Grimble et al[24]	1988	104	Healthy; pre- and postsurgical	Adults	TPN 73% ± 16; range 25–95% TEN 81% ± 13; range, 57–109% Fasted 84% ± 10; range, 74–100% Fed 87% ± 9; range 74–100%
Loder et al[27]	1989	120	Pre- and postsurgical		25% error postsurgical
Helms et al[30]	1991		Pre- and postsurgical	Neonates	57% ± 4 postop day 1 40.6% ± 16 postop day 2
Akin	1991	25	ICU	72 h–4 wk	Range, 0.8–69.0%
Konstantinides et al[25]	1991	491	Trauma and postoperative		Overall, 80 ± 12%; range, 12–112% Nitrogen balance range, 0.1–12 g Difference UUN versus TUN
Moore et al[31]	1991	99	BMT	Adults	Urea acceptable in most patients after BMT
Konstantinides et al[26]	1992	27	Burn	Adults	63 ± 12%
Boehm (personal communication)	1992	46	Neonates		47.2 ± 16.2%
Boehm (personal communication)	1992	92	Critically ill	Pediatrics	62.5 ± 21.9%

* Publication of studies that examine the validity of UUN against TUN in various populations of hospitalized patients under stress conditions. ICU, intensive care unit; Postop, postoperative; BMT, bone marrow transplantation.

urea production can be attributed to disease-specific causes such as cirrhosis or liver failure, in which less urea is produced from ammonia, the by-product of catabolism (amino acids).[33]

Grimble et al[24] have summarized many metabolic alterations that could result in a lowered UUN/TUN ratio. The following is an excerpt from their report.

Several explanations may be suggested for low UUN/TUN. Total starvation[34] and chronic protein and energy restriction[35] result in conservation of nitrogen and a switch to ketones as a metabolic fuel.[36] Ureagenesis is depressed while ammonia excretion increases markedly, as a result of the need to titrate urinary ketone losses with NH_4^+[35] derived from glutamine.[37] Alterations in UUN/TUN, under these circumstances, are quite marked, in one study protein restriction reduced UUN/TUN to 68% after 8 day,[35] while 6 weeks' starvation caused UUN/TUN to fall to 33%.[34] In chronic acidosis, a similar pattern occurs due to increased renal uptake of glutamine.[38] Similar considerations would apply to the pattern of urine nitrogen excretion in the severely malnourished, acidotic, or cachexic patient. Although aminoaciduria accounts for only 0.5–2.5% of urine nitrogen,[35,39] as with creatinine,[34] a decline in urea excretion will alter UUN/TUN markedly even though amino acid and creatinine excretion have not increased greatly.[40] Finally, where there is extensive catabolism of connective tissue, proline/hydroxyproline-containing peptides released are not reabsorbed by the kidney[41] but can appear in large quantities in the urine, and represent a not inconsiderable nitrogen loss.[42,43]

Although urea production may be altered, measured UUN and other metabolic indices, as shown in Table 4,[44] can aid in determining stress levels and in prescribing and monitoring the protein and nutritional treatment regimen. UUN reflects the rate of muscle catabolism, that is, primary lean body mass. TUN reflects UUN and other by-products of the catabolism, which is both accelerated and occurs excessively in the hypermetabolic period accompanying stress.

Steinhorn et al found that urinary urea averaged only 45.7 ± 0.6% of the measured TUN in intensive care unit pediatric patients during the first day of stress after a surgical procedure.[28] They also showed that liver failure and/or sepsis can alter urea production and invalidate the use of UUN in the same population.[29]

Grimble et al also reported deviation from the normal 80% in both enterally and parenterally fed adult surgical patients during the first 3 days after surgery.[24] Patients receiving TPN had UUN/TUN ranging from 25% to 95% (72.7 ± 15.8%). The enterally fed patients had UUN/TUN ratios ranging from 57% to 109% (80.5 ± 13.3%). For meaningful comparison, two control groups were also included in the study. Group 1 fasted, and group 2 was fed. The UUN/TUN values for the two

Table 4. Categories of metabolic stress*

	Concentration in Plasma (μmol/L)					Concentration in Urine (μmol/L)	
Stress	Lactate†	Glucose‡	Leucine	Proline	Phenylalanine	Nitrogen (g/d)	3-Methyl Histidine
0	<1000	5.5 ± 2	120 ± 10	200 ± 20	60 ± 15	<5	<100
1	1200 ± 200	9.5 ± 1.4	74 ± 12	213 ± 4	74 ± 8	5–10	130 ± 20
2	1200 ± 200	9.5 ± 1.4	74 ± 12	13 ± 40	74 ± 8	10–15	200 ± 20
3	3000 ± 500	16 ± 1.6	180 ± 30	300 ± 50	124 ± 17	>15	450 ± 50

* Reproduced with permission from Konstantinides et al.[44]
† In the presence of lactate/pyruvate, ratio less than 20.
‡ In the absence of steroid therapy, diabetes mellitus, or pancreatitis.

groups were 87.0 ± 9.3% and 84.0 ± 10.2%, respectively, with moderately varying ranges of 74% to 100% in group 1 and 70% to 100% in group 2.

Ward and colleagues[45] examined the effects of nitrogen delivery comparing the route of delivery in general surgical patients and found results similar to those of Grimble et al.[46] In their population, Ward et al observed that TPN-fed patients had a mean UUN/TUN of 87% (range, 30% to 90%), whereas the TEN patients had a mean UUN/TUN of 83.8% (range, 55% to 100%).

Loder et al focused on the relationship between UUN and TUN in preoperative, postoperative, and critically ill patients.[27] In their study, UUN and TUN were closely related in preoperative patients. Postoperative and stressed patients exhibited UUN/TUN inconsistencies within each group, producing unreliable estimates of the nonurea nitrogen excretion from individual patients.

Helms and colleagues[46] recently conducted a study of postsurgical, preterm neonates receiving parenteral nutrition. They concluded that TUN assessment of nitrogen loss is a more accurate method for evaluating nitrogen balance. They based their reasoning on the fact that UUN assessment was associated with wide intrapatient and interpatient variability leading to a significant underestimation of nitrogen loss.

Konstantinides et al retrospectively studied the relationship between UUN and TUN in stressed patients, most commonly surgical or trauma patients.[25] Samples were collected and studied over a range of 1 to 10 days after the stressful event had occurred. The population studied was composed of members from each sex who were not insulin-dependent diabetics or cirrhotic and who displayed an adequate glomerular filtration rate (creatinine clearance > 25 mL/min). Four hundred ninety-one UUN/TUN paired studies were performed with measured TUN outputs ranging from 0.04 to 54.0 g/d. The UUN/TUN ratio for the entire population was 80.0 ± 12.0%. In this patient population, the range varied from 12 to 112% (Fig 1). Data from 315 nitrogen balance studies were used to compare nitrogen balance determined by using UUN as an estimate of TUN (corrected by 1.25 [times] UUN) with those calculated directly from measured TUN. The difference between these two groups was 1.85 ± 1.69 g, with a range of 0.01 to 12.31 g (Fig 2). Only the parenteral route of administration of nutrition was used in this study. When results for UUN/TUN were examined for the effect of nitrogen input, there appeared to be an upward trend in urea production as nitrogen input was increased but no statistically significant differences were found. Similar results were found for the nitrogen balance studies.

There is little difference in UUN/TUN or nitrogen balance at the lower end of TUN output or low stress level. There is a progressively increasing difference in the UUN/TUN and likewise nitrogen balance as the TUN output or the degree of stress increases.

PYROCHEMILUMINESCENCE™

The Kjeldahl procedure is the most widely used method for measuring nitrogen in analytical chemistry. Application of this method for measuring TUN in supportive nutrition assessment has been criticized as being costly, hazardous, and time consuming. Today, the current micro-Kjeldahl method is safer than the older technology, and although it is expensive and slow, it remains in many clinical laboratories for measuring TUN. Pyrochemiluminescence (PCL) (Antek Instruments Inc, Houston, TX) has been proposed as an

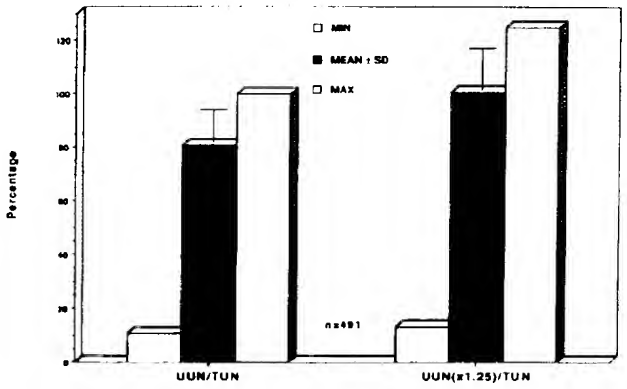

Figure 1. Comparison of UUN/TUN ratios and corrected UUN/TUN ratios for nonurea nitrogen components. Reproduced with permission from Konstantinides et al.[25]

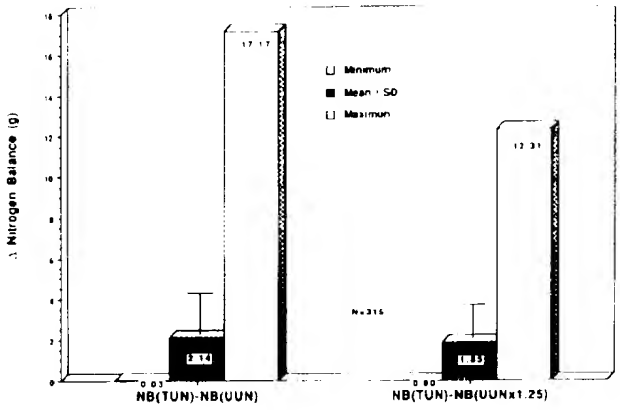

Figure 2. Change in nitrogen balance (NB), expressed in grams, calculated from NB using TUN, UUN, and estimated TUN (as UUN x 1.25). Reproduced with permission from Konstantinides et al.[25]

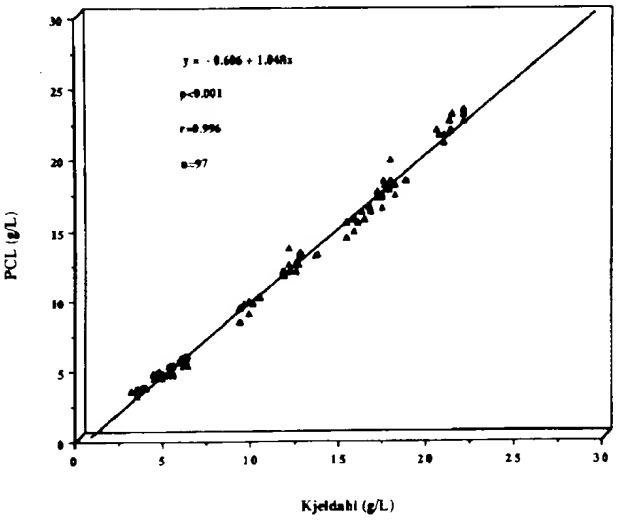

Figure 3. Regression analysis of PCL versus Kjeldahl for TUN determinations for 24-hour urine collections over entire range measured: $r = .996$; $r^2 = .992$; n = 97; y = 2.048 x -0.606 ($P < .001$). Reproduced with permission from Konstantinides et al.[17]

alternative to the Kjeldahl method for TUN measurement in support of nutrition assessment in clinical laboratories. PCL was first used in 1977 in the petrochemical industry to determine the nitrogen content of petroleum products. Shortly thereafter, Ward et al, using a modified chemiluminescence analyzer, were able to adapt the concepts to measure nitrogen in biological fluids. Konstantinides et al compared the time and cost effectiveness of TUN analysis by PCL versus traditional Kjeldahl techniques as well as the linear regression between the two methods.[17] The results suggest a significant savings in both time and cost by PCL, with an excellent regression between urine samples analyzed by both methods (Fig 3). Many investigators have studied the relationship between biological samples measured by micro- and macro-Kjeldahl methods versus PCL and have concluded that PCL is a cost-effective alternative in determining nitrogen content[24,25,45,47,52] (Table 5). It is now well established that PCL can replace the Kjeldahl procedure in clinical laboratories when TUNs are performed for nitrogen balance determinations in the clinical setting.

CREATININE-HEIGHT INDEX

Creatinine is a component of urine nitrogen that is a waste product of creatine. The formation of creatinine is constant and represents 1.7% to 2.0% of the creatine produced. Creatinine is also a by-product of phosphocreatine, a high-energy phosphate formed by creatine that is used in muscle metabolism.[53] In 1976, Forbes and Bruining investigated the relationship between urinary creatinine and lean body mass.[54] Their subjects were 13 short-statured children and 21 normal adults. None of the subjects were receiving medications or had any evidence of urinary tract disease. Three 24-hour urine collections were made for each subject. Lean body mass was plotted against average creatinine with a correlation coefficient of 0.988. Forbes and Bruining concluded that urinary creatinine excretion may serve as a reasonable index of lean body mass in subjects without dietary restrictions.

A similar study, conducted by Heymsfield et al, reached the same conclusions but with added stipulations.[55] First, changes from a creatinine-free diet to a meat diet and vice versa cause changes in the amount of creatine and, hence, urinary creatinine excretion. Variability in creatinine excretion also can be attributed to normal daily variation, severe emotional stress, vigorous exercise, different phases of the menstrual cycle, severe renal insufficiency, and severe illness. It was concluded that the use of creatinine as an index of muscle mass should serve only as an approximation. These qualifications limit the usefulness of creatinine excretion to a select group of individuals.

The assessment of urinary creatinine is often accompanied by the use of the creatinine-height index. Creatinine-height index is the 24-hour creatinine excretion of the patient divided by the expected 24-hour creatinine excretion of a normal adult of the same height. It is the ratio between observed and expected urinary creatinine values. Expected creatinine is calculated by finding the expected creatinine level of a well-nourished person based on height. Supplements to the patient's nutritional program may be made accordingly.

In 1970, Viteri and Alvarado studied the accuracy of the creatinine-height index in the estimation of protein status in malnourished children.[56] Several children classified as having edematous protein calorie malnu-

Table 5. Pyrochemiluminescence (PCL) versus Kjeldahl for biological samples*

Author/Ref no.	Journal	Year	Experiment	Sample	Conclusion
Ward et al[45]	Clin Chem	1980	PCL versus Kjeldahl	Biological	$r = 0.99, 0.96, 0.72$; PCL acceptable
Drummond et al[48]	JPEN	1986	PCL versus Kjeldahl	Urinary nitrogen	$r = 0.97$; PCL acceptable
Grimble et al[24]	JPEN	1988	PCL versus Kjeldahl	Fecal and urinary	Fecal $r = 0.96$; PCL acceptable
Konstantinides et al[47]	Clin Chem	1988	PCL versus Kjeldahl	Urine	$r = 0.996$; PCL acceptable
Konstantinides et al[15]	JPEN	1989	PCL versus Kjeldahl	Urine	$r = 0.996$; PCL acceptable
Konstantinides	ESPEN	1989	PCL versus Kjeldahl	Urine	$F = 0.482$, $P = 0.695$; multicenter comparison shows no difference
Dechert et al[50]	JPEN	1990	PCL versus Kjeldahl	Urine	$r = 0.97$; PCL acceptable
Skogerboe et al[51]	Clin Chem	1989	PCL versus Kjeldahl	Homogenized food or stool	$r = 0.999, 0.998$; PCL acceptable
Skogerboe et al[52]	Clin Chem	1990	PCL versus Kjeldahl for TUN	Urine	$r = 0.975$; PCL acceptable

* Publication/presentations of studies that examine the validity of PCL against Kjeldahl methods for measuring nitrogen levels in various biological samples.

trition and nonedematous protein calorie malnutrition were kept under careful pediatric care. Twenty-four hour urine samples were collected when adequate urinary flow had been established. The children received a strict diet, with 20% of the calories derived from fat in milk and vegetable oil and the rest provided by protein, sucrose, dextromaltose, and starch. It was concluded that the creatinine-height index accurately reflected the degree of protein depletion and repletion in the hospitalized children. A main limitation was the preferred requirement of a 72-hour urine collection.

Bistrian et al also studied nutritional depletion in hospitalized patients.[56] The creatinine-height index was calculated for 30 young, adult male students who were fed meat-free diets that supplied adequate protein. This was compared with the creatinine-height index of 11 malnourished male surgical patients. The mean creatinine-height index was 1.09 in the young, adult males and 0.50 in the malnourished surgical patients. Bistrian et al concluded that these results suggest a role for the creatinine-height index in the nutrition assessment of the surgical patient.

SUMMARY

Nitrogen balance studies play an important role in the nutrition and metabolic management of hospital patients. Nitrogen excretion can be effectively measured using urine kept on ice or at room temperature, with or without preservatives. Twenty-four-hour urine collections are preferred rather than those of shorter duration. Urine is analyzed for UUN or TUN, although TUN offers more advantages.

Under nonstressed conditions, urea composes 80% to 90% of TUN but, with increased stress in a variety of age groups, has been found to vary from 10% to 90%. Nitrogen excretion calculated from UUN is affected by increased stress, which can alter urea production and/or increase nonurea nitrogen by-products. Therefore, TUN results are consistently more reliable. Because the technology is available to quantify TUN by PCL, it remains the preferred method of urinary nitrogen excretion determination for hospitalized patients, especially those with increased stress.

ACKNOWLEDGMENTS

The author thanks C. N. Moga, BS, for his literature search and background data; M. S. Garland for his assistance in preparing this document; Nancy N. Konstantinides, RN, MS, CNSN, for her editorial review of the manuscript; and Professor Frank B. Cerra, MD, for his comments on the manuscript.

REFERENCES

1. Randall HT. The history of enteral nutrition. In: Rombeau JL, Caldwell MD, eds. Enteral and tube feedings. Vol 1. Philadelphia: WB Saunders Co, 1984:1-9.
2. Dudrick SJ, Wilmore DW, Vars HM, et al. Long-term total parenteral nutrition with growth development and positive nitrogen balance. Surgery 1968;64:134-42.
3. Dudrick SJ, Wilmore DW, Vars HM, et al. Can intravenous feeding as a sole means of nutrition support growth in the child and restore weight loss in an adult? An affirmative answer. Ann Surg 1969;169:974.
4. Cerra FB, Lehman S, Konstantinides NN, et al. Effect of enteral nutrient on in vitro tests of immune function in ICU patients: a preliminary report. Nutrition 1990;1:84-7.
5. Blackburn GL, Bistrian BR, Maini BS, et al. Nutritional and metabolic assessment of the hospitalized patient. JPEN 1977; 1:11-22.

6. Cerra FB. Profiles in nutritional management: the trauma patient. Chicago: Medical Directions, Inc. 1982.
7. Phinney SD. The assessment of protein nutrition in the hospitalized patient. Clin Lab Med 1981;1:767-74.
8. Wilmore DW. The metabolic management of the critically ill. New York: Plenum Medical Book Co, 1977:193-4.
9. Bingham SA, Cummings JH. The use of creatinine output as a check on the completeness of 24-hour urine collections. Hum Nutr Clin Nutr 1985;39C:343-53.
10. Forbes GB, Bruining GJ. Urinary creatinine excretion and lean body mass. Am J Clin Nutr 1976;29:1359-66.
11. Heymsfield SB, Arteaga C, McManus C, et al. Measurement of muscle mass in humans: validity of the 24-hour urinary creatinine method. Am J Clin Nutr 1983;37:478-94.
12. Gibson RS. Principals of nutritional assessment. New York: Oxford University Press, 1990:307-47.
13. Waxman K, Rebello T, Pinderski, et al. Protein loss across burn wounds. J Trauma 1987;2:136-40.
14. Konstantinides FN, Fath JJ, Scanlan S, et al. 24-hour urine collection for nitrogen balance: is iced collection necessary? Nutr Supp Serv 1985;5(9):34-7.
15. Konstantinides FN, Sackett-Lundeen L, Mitchell DR, et al. The effects of methods for 24-hour urinary catecholamine collection on nutritional parameters in clinical practice [abstract]. JPEN 1989;13:21S.
16. Zlatnik FJ. Urinary urea nitrogen ratios. J Reprod Med 1981;26:119-21.
17. Konstantinides FN, Fath JJ, Kajander SP, et al. Stability of frozen urine for nitrogen balance assessment. Nutr Supp Serv 1987;7(12):30-1.
18. Candio JA, Hoffman MJ, Lucke JF. Estimation of nitrogen excretion based on abbreviated urinary collections in patients on continuous parenteral nutrition. JPEN 1991;15:148-51.
19. Quandt CM, Horst HM, Obeid FN, et al. Accuracy of two-hour urine urea nitrogen determinations in critically ill patients. Clin Pharm 1984;3:408-11.
20. Record KE, Richards VR, Bell RM. Calculating nitrogen balance from urine samples collected over six hours. Clin Pharm 1984; 3:76-7.
21. Ford EG, Jennings LM, Andrassy RJ. Hourly urine nitrogen values do not reflect 24-hour totals in injured children. NCP 1987;2:195-8.
22. Lopez AM, Wolfsdorf J, Raszynski A, et al. Estimation of nitrogen balance based on a six-hour collection in infants. JPEN 1986;10:517-8.
23. Sorkness R. The estimation of 24-hour urine urea nitrogen excretion from urine collections of shorter duration in continuously alimented patients. JPEN 1984;3:300-1.
24. Grimble GK, West MFE, Acuti ABC, et al. Assessment of an automated chemiluminescence nitrogen analyzer for routine use in clinical nutrition. JPEN 1988;12:100-6.
25. Konstantinides FN, Konstantinides NN, Li JC, et al. Urinary urea nitrogen: too insensitive for calculating nitrogen balance in clinical nutrition. JPEN 1991;15:189-93.
26. Konstantinides FN, Radmer WJ, Becker WR, et al. Inaccuracy of nitrogen balance determinations in thermal injury with calculated total urinary nitrogen. J Burn Care Rehab 1992;13(2):254-60.
27. Loder PB, Kee AJ, Horsburgh R, et al. Validity of urinary urea nitrogen as a measure of total urinary nitrogen in adult patients requiring parenteral nutrition. Crit Care Med 1989;17:309-12.
28. Steinhorn D, Radmer W. Urea synthesis is not consistent throughout the acute phase of stress. JPEN 1986;10:11S.
29. Steinhorn D, Radmer W, Weisdorf S. Altered urinary nitrogen excretion in sepsis and liver failure in critically-ill children. Ped Res 1985;19:146A.
30. Helms RA, Mowatt-Larrsen CA, Christensen ML, et al. Urinary nitrogen constituents in the preterm neonate on TPN [abstract]. JPEN 1991;15:25S.
31. Moore R, Havala T, Kaproth P, et al. Urinary urea nitrogen is predictive of total urinary nitrogen in bone marrow transplant patients [abstract]. JPEN 1991;15:32S.
32. Wette HC, Rettmer R, Grube BJ, et al. Nitrogen balance in acute thermal injuries: TUN vs. UUN in calculations. Proc Am Burn Assoc 1990;22.
33. Krevsky B, Godley J. Nutrition support in advanced liver disease. Nutr Supp Serv 1985;5:8-17.
34. Owen OE, Felig P, Morgan AP, et al. Liver and kidney metabolism during prolonged starvation. J Clin Invest 1969;48:574-83.
35. Vinnars E. Effect of intravenous amino acid administration on nitrogen retention. Scand J Clin Lab Invest 1971;27(suppl 117):1-56.
36. Cahill GF Jr. Starvation in man. N Engl J Med 1970;282:668-75.
37. Alleyne GAO, McFarlene-Anderson N, Lupianez JA, et al. Metabolism of ammonia. In: Waterlow JC, Stephen JML, eds. Nitrogen metabolism in man. London: Applied Science Publishers, 1981:169-92.
38. Owen OE, Robinson RR. Amino acid extraction and ammonia metabolism by the kidney during prolonged administration of ammonium chloride. J Clin Invest 1963;42:263-76.
39. Jacobson S. Serum concentrations and urinary excretion of amino acids during parenteral nutrition after abdominal surgery. JPEN 1982;6:204-13.
40. Wannemacher RW, Dinterman RE, Pekarek RS, et al. Urinary amino acid exretion during experimentally induced sandfly fever in man. J Clin Nutr 1975;28:110-8.
41. Prockop DJ, Sjoerdsma A. Significance of urinary hydroxyproline in man. J Clin Invest 1962;40:843-9.
42. Faull KF, Schlesinger P, Halpern B. The mass spectrometric identification of dipeptides in the urine of a patient suffering from chronic ulceration and oedema. Clin Chem Acta 1976; 70:313-21.
43. Carpentier C, Johnstone RAW, Lemonnier A, et al. Analysis of dipeptides in urine by gas chromatography/mass spectrometry: implications for collagen breakdown in iminopeptidura following the study of dipeptides by electron impact and chemical ionisation. Clin Chem Acta 1984;138:299-308.
44. Konstantinides FN, Kaproth PL, Cerra FB. Other aspects of metabolic monitoring in critically ill patients. Clin Chem 1990;36:1594-603.
45. Ward MWN, Owens CWI, Rennie MJ. Nitrogen estimation in biological samples by use of chemiluminescence. Clin Chem 1980;26:1336-9.
46. Helms RA, Alvarado-Hughes M, Fernandes ET, et al. Nitrogen balance determinations in preterm neonates [abstract]. JPEN 1989;13:19S.
47. Konstantinides FN, Boehm KA, Radmer WJ, et al. Pyrochemiluminescence: real-time, cost-effective method for determining total urinary nitrogens in clinical nitrogen-balance studies. Clin Chem 1988;34:2518-20.
48. Drummond RW, Mazzagatti L, Guthrie PD. Evaluation of a chemiluminescence nitrogen analysis technique for use in nutritional assessment studies [abstract]. JPEN 1986;10:19S.
49. Konstantinides FN, Li JC, Rettmer RL, et al. A multicenter comparison of TUNs for NB studies measured by PCL. Clin Nutr 1989:8S:78.
50. Dechert RE, Cerny JC, Bartlett RH. Measurement of elemental nitrogen by chemiluminescence: An evaluation of the Antek nitrogen analyzer system. JPEN 1990;14:195-7.
51. Skogerboe KJ, McLaughlin MK, Labbe RF. Comparison of sample preparation techniques for measurement of total nitrogen in stool and food samples by chemiluminescence. Clin Chem 1989;35:1114.
52. Skogerboe KJ, Labbe RF, Rettmer RL, et al. Chemiluminescent measurement of total urinary nitrogen for accurate calculation of nitrogen balance. Clin Chem 1990;36:752-5.
53. Heymsfield SB, Arteaga C, McManus C, et al. Measurement of muscle mass in humans: validity of the 24-hour urinary creatinine method. Am J Clin Nutr 1983;37:478-94.
54. Forbes GB, Bruining GJ. Urinary creatinine excretion and lean body mass. Am J Clin Nutr 1976;29:1359-66.
55. Viteri FE, Alvarado J. The creatinine height index: its use in the estimation of the degree of protein depletion and repletion in protein calorie malnourished children. Pediatrics 1970;46:696-706.
56. Bistrian BR, Blackburn GL, Sherman M, et al. Therapeutic index of nutritional depletion in hospitalized patients. Surg Gynecol Obstet 1975;141:512-6.